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Original Article

The effectiveness of peroneal nerve stimulation combined with neuromuscular electrical stimulation in the management of knee osteoarthritis: A randomized controlled single-blind study

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ABSTRACT

Objectives: This study aimed to compare the effectiveness of neuromuscular electrical stimulation (NMES) combined with peroneal nerve stimulation (PNS) on muscle strength around the knee, proprioception, pain, functional status, and quality of life in patients with knee osteoarthritis (OA).

Patients and methods: The prospective, randomized, single-blinded, controlled trial included 63 patients with clinical and radiological diagnoses of knee OA between December 2019 and March 2020. The patients were divided into two groups: Group 1 (NMES+PNS, n=31) and Group 2 (NMES, n=32). The patients were followed up at two and six weeks. Main outcome measures were the Visual Analog Scale, Western Ontario and McMaster Universities Arthritis Index, Nottingham Health Profile, and 100-m walking test, quadriceps muscle strength, hamstring muscle strength (HMS), and joint position sense were evaluated using a computer-controlled isokinetic dynamometer at 60°/sec, 90°/sec, and 120°/sec angular velocities. The proprioception was evaluated at 30° and 60° flexion angles using the same device.

Results: Two patients from Group 1 and two patients from Group 2 were excluded from the study after they failed to show up for the six-week control. As a result, the study was completed with 59 patients (30 females, 29 males; 55.9±6.1 years; range, 40 to 65 years). There was a significant difference between the two groups in the 100-m walking test parameter at the six-week control in favor of Group 1 ($p<0.05$). There was a significant difference in favor of Group 1 in the parameters of proprioception (30° and 60°) and HMS (60° and 90°) in both the two-week evaluation and six-week controls ($p<0.05$). The HMS 120° parameter showed a significant difference in favor of Group 1 at the six-week control ($p<0.05$).

Conclusion: In patients with knee OA, we believe that PNS combined with NMES may be more effective than NMES treatment alone in terms of proprioception, HMS, and functional status.

Keywords: Exercise, isokinetic dynamometer, knee osteoarthritis, neuromuscular electrical stimulation, peroneal nerve stimulation, proprioception.

Osteoarthritis (OA) is a degenerative joint disease that frequently affects weight-bearing joints.[1] This condition impairs one's quality of life while also causing a loss of function.[1] Joint usage declines because of pain due to OA. Thus, inactivation develops in the muscles around the knee, particularly in the quadriceps.[2] As a result, improving muscle strength is an effective treatment method for patients with knee OA to reduce or stop the progression of the condition.[3]

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Arthrogenic muscle inhibition is a condition that prevents complete contraction of the muscle via transmission of inhibitory impulses to the alpha motor neurons of the muscles affected due to pain and injury in the joint.[4] Various studies have shown that arthrogenic muscle inhibition causes muscle weakness and atrophy in OA.[5,6] Furthermore, muscle weakness or atrophy can lead to reduced muscle spindle sensitivity and impaired proprioception.[7]

The main treatment for preventing muscle atrophy and increasing strength is exercise. Isotonic, isometric, and isokinetic exercises are used for this purpose.[8] Neuromuscular electrical stimulation (NMES) improves functionality by reducing joint stiffness while also enhancing muscle strength.[5] Therefore, it is considered an alternative treatment for patients who cannot adapt to an exercise regimen or have contraindications.[9]

Peroneal nerve stimulation (PNS) is considered to prevent arthrogenic muscle inhibition by limiting inhibitory impulse transmission to the alpha motor neurons of the quadriceps; this reduces muscular atrophy and prevents loss of strength.[10]

The goal of our study was to demonstrate the efficacy of NMES combined with PNS since their individual efficiencies have been shown in earlier studies. We compared the effects of exercise and NMES combined with PNS on quadriceps muscle strength (QMS), hamstring muscle strength (HMS), and proprioception in patients with knee OA to determine a more effective and advantageous treatment program. In addition, we aimed to compare the effectiveness of these treatments on pain, functional status, and quality of life of patients.

PATIENTS AND METHODS

The prospective, single-blinded, randomized controlled study included patients who visited the Physical Medicine and Rehabilitation Outpatient Clinic of the Bursa Yüksek Ihtisas Training and Research Hospital between December 2019 and March 2020 due to knee pain and were diagnosed with knee OA according to the American College of Rheumatology (ACR) criteria. The patients included in the study were selected according to the following inclusion criteria: diagnosis of primary knee OA according to ACR-endorsed criteria,[11] age >18 years, radiographs taken within the last year showing Grade 2 or 3 knee OA according to the Kellgren-Lawrence Grading Scale, having knee pain for more than six months. The exclusion criteria were as follows: a history of knee trauma, surgical operation to the knee area, intra-articular steroid or hyaluronate administration to the knee joint, physical therapy for the knee, and use of nonsteroidal anti-inflammatory drugs on a regular basis in the last six months, acute synovitis, neurological deficit in the lower extremity, inflammatory diseases, inadequate general health (heart failure, advanced asthma, or history of malignancy), any condition that has the potential to cause polyneuropathy, and conditions that may contraindicate electrical stimulation (pacemaker, skin irritation, wound, or infection).

The study comprised 63 patients who met the inclusion criteria. Patients were randomized into two groups using the random number table. The random number table was produced with the Random Integer Generator procedure from the website http://www.random.org/. It generated 100 random integers. Sequentially, numbered index cards with the random assignments were prepared and placed in envelops. These patients were classified into two groups by the investigator who opened the envelopes to attribute the interventions [Group 1 (NMES+PNS, n=32) and Group 2 (NMES, n=31)]. The demographic data were recorded. The same physician administered all the treatments. The patients were evaluated by another physician blinded to the treatment. Evaluations were made before treatment, immediately after treatment (second week), and at six weeks after treatment.

Both groups of patients were given a home exercise regimen to strengthen the muscles around the knees. The duration of exercise in both groups was six weeks.[12] The patients were given knee range of motion and stretching exercises for the first three weeks, then quadriceps and hamstring strengthening exercises were added for the remaining three weeks to these exercises. The exercises were applied twice a day with 15 repetitions for six weeks. It was progressively increased to 20 repetitions if the patient could endure it.[13]

Neuromuscular electrical stimulation was performed five times a week (10 sessions in total) for two weeks for the affected knee of the 31 patients in Group 1. It was performed for 22 min in the rehabilitation mode using the Compex MI Sport (DJO France, Mouguerre, France) four-channel, 120 mA, 60-400 μsec, 150 Hz device. Stimulation was performed with the patient seated and the knee flexed to 90°. The patient was instructed to

actively raise the knee to a complete extension when muscle contractions began and then return to the 90° flexion position when the contraction ended. Stimulation intensity was increased up to a level that the patient could endure and the muscle contractions were visible. Patients in this group also received PNS. The Chattanooga Intelect Advanced (DJO France, Mouguerre, France) device was used for PNS with Russian stimulation and 10-sec current and 50-sec rest periods. The superficial (cathode) electrode was placed on the common peroneal nerve at the level of the fibular head, and the reference (anode) electrode was placed 2 cm away from the cathode. The maximum amount of current that the patients could tolerate was used for PNS until dorsiflexion in the ankle was seen. Except for PNS, all other procedures performed for patients in Group 2 were identical to those performed for patients in Group 1.

Primary outcome measures

Isokinetic evaluation for muscle strength measurement (Newton-meter [Nm]) was performed using a computer-controlled isokinetic dynamometer (Cybex HUMAC/NORM, model no: 502140; CSMI, Stoughton, MA, USA).[14] Each time the device was powered on, a calibration was conducted prior to evaluation. Three tries at angular speeds of 60°/sec, 90°/sec, and 120°/sec were performed in accordance with the test protocol to prepare the patients for the test before starting the recordings, and the main protocol was started after knee flexion and extension were performed. Before the procedure, the patient's leg weight was assessed by the device, and the influence of gravity was rectified by it; this was considered during force calculations. The effect of gravity on the torque was calculated by the device at 45°. The torso and leg were stabilized with tapes. With the help of a pad, the leg was tied over the malleolus. The rotation axis of the dynamometer was brought to the level of the lateral femoral condyle. Isokinetic muscle strength measurements for knee flexion and extension were performed at 60°/sec, 90°/sec, and 120°/sec angular velocities for five repetitions. In a sitting position, measurements were taken with the hips flexed to 90°. Information regarding the goal, device, and application of the test was provided to the patients before the test, and the patients were motivated verbally during the test.

Proprioception was assessed by the patient's sense of joint position. The patients' ability to actively locate the joint position, which was previously taught passively, was used to assess their sense of joint position.[15] The Cybex HUMAC/NORM isokinetic dynamometer was used for this purpose. While the knee was slowly brought from 90° flexion to passive

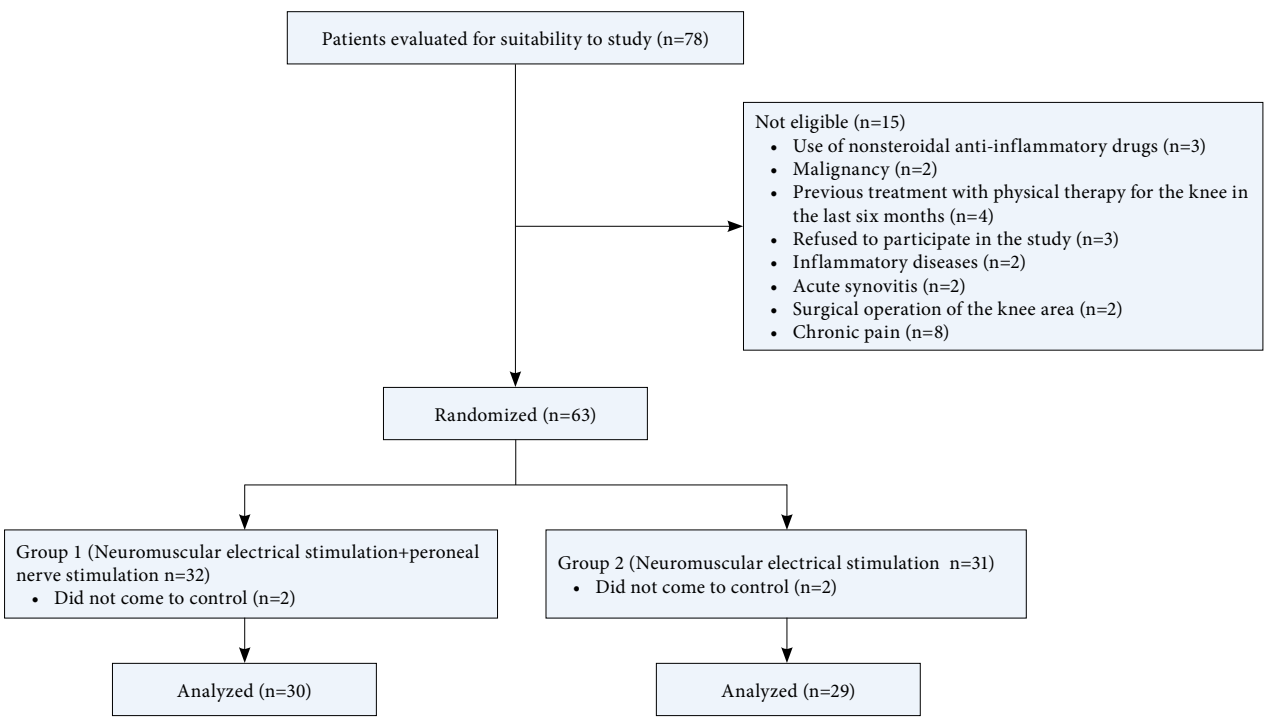

Figure 1. Flow diagram of the study.

extension, it was paused for 10 sec each at 60° and 30° flexion angles, and the patient was taught these angles. The knee was then raised back to 90° flexion, and the subjects were instructed to find the taught angles. The patients tried to determine these angles by actively moving their knees from this starting position to the previously taught 60° and 30° flexion angles. The angles that the subjects were taught and the angles that they found were both recorded. Three repetitions at all angles were used to calculate the mean.

Secondary outcome measures

A 10-cm Visual Analog Scale (VAS) was used to evaluate pain severity (0= no pain, 10= very severe pain).[16]

Pain, joint stiffness, and functional status were assessed using the Western Ontario and McMaster Universities Arthritis Index (WOMAC), which consists of 24 questions. Each question was graded on a scale of one to five. A high score indicated poor health, whereas a low score indicated good health.[17]

TABLE 1
Comparison of the demographic characteristics and pretreatment evaluation parameters of the baseline data between the two groups

	Group 1 (NMES+PNS) (n=30)			Group 2 (NMES) (n=29)			
	n	Median	Min-Max	n	Median	Min-Max	*p*
Age (year)		56	40-65		58	47-65	0.970
Sex							0.480
Female	25			5			
Male	20			9			
Body mass index (kg/m^2)		31.2	22.5-37.4		30	20.1-35.1	0.111
Kellgren-Lawrence Grading							0.902
Grade 2	14			15			
Grade 3	16			14			
Visual Analog Scale		6.5	3-9		6	3-9	0.187
100 meter walk test		67	48-85		74.5	50-86	0.780
PRS 30° (0)		37.6	27.3-52.6		42	24.6-56.6	0.103
PRS 60° (0)		62.3	43.3-71.3		63	48-75.3	0.278
QMS 60° (Nm)		58	30-113		61	24-116	0.509
QMS 90° (Nm)		45.5	25-110		52	21-81	0.086
QMS 120° (Nm)		40.5	19-80		46	24-88	0.081
HMS 60° (Nm)		30.5	15-88		37	16-72	0.610
HMS 90° (Nm)		25.5	16-60		31	11-64	0.650
HMS 120° (Nm)		23	11-56		28	16-51	0.620
WOMAC Pain		8	3-18		10	1-14	0.593
WOMAC Stiffness		2	0-6		2	0-5	0.890
WOMAC Physical function		27	7-53		25	6-47	0.595
WOMAC Total		40.1	10.4-79.1		40.6	8.3-63.5	0.891
NHP Pain		52.3	25.2-100		48.9	14.7-100	0.980
NHP Emotional reactions		57	0-92.7		52.8	0-100	0.873
NHP Sleep		46.1	0-77.6		27.2	0-77.6	0.710
NHP Social isolation		7.9	0-100		22.5	0-58.1	0.818
NHP Physical activity		32.5	0-54.4		41.8	10.79-67.1	0.272
NHP Fatigue		76	0-100		63.2	0-100	0.258
NHP Total		278	72-512		239	111-476	0.192

NMES: Neuromuscular electrical stimulation; PNS: Peroneal nerve stimulation; PRS: Proprioception; QMS: Quadriceps muscle strength; Nm: Newton-meter; HMS: Hamstring muscle strength; WOMAC: Western Ontario and McMaster Universities Arthritis Index; NHP: Nottingham health profile.

TABLE 2
Intragroup comparison of posttreatment (two and six weeks) values

	Pre-treatment (W0)		Second week (W2)		Sixth week (W6)		W0-W2	W0-W6
	Median	Min-Max	Median	Min-Max	Median	Min-Max	*p*	*p*
VAS								
Group 1 (NMES+PNS)	6.5	3-9	4	0-8	4	0-9	**<0.001**	**<0.001**
Group 2 (NMES)	6	3-9	4	0-7	5	0-9	**<0.001**	**<0.001**
100 meter walk test								
Group 1 (NMES+PNS)	67	48-85	63	45-75	62	46-77	**<0.001**	**<0.001**
Group 2 (NMES)	74.5	50-86	67	47-80	61	48-78	**<0.001**	**<0.001**
Proprioception 30° (0)								
Group 1 (NMES+PNS)	37.65	27.3-52.66	36.16	26.66-46	36.16	24-46	**0.038**	0.074
Group 2 (NMES)	42	24.66-56.66	33.33	24-44	31.33	22-40	**<0.001**	**<0.001**
Proprioception 60° (0)								
Group 1 (NMES+PNS)	62.33	43.33-71.33	59.16	44-70	60	45-68	0.104	0.108
Group 2 (NMES)	63	48-75.33	58.66	48-65.33	59.33	49-66	**<0.001**	**<0.001**
QMS 60° (Nm)								
Group 1 (NMES+PNS)	58	30-113	70.5	39-96	66.5	45-111	**0.020**	**0.041**
Group 2 (NMES)	61	24-116	73	41-126	74	43-123	**0.004**	**<0.001**
QMS 90° (Nm)								
Group 1 (NMES+PNS)	45.5	25-110	49.5	36-85	58.5	38-87	**0.030**	**0.005**
Group 2 (NMES)	52	21-81	59	42-104	60	37-113	**0.001**	**<0.001**
QMS 120° (Nm)								
Group 1 (NMES+PNS)	40.5	19-80	53.5	24-71	51	30-68	**0.008**	**0.005**
Group 2 (NMES)	46	24-88	50	32-85	54	26-89	**0.047**	**0.002**
HMS 60° (Nm)								
Group 1 (NMES+PNS)	30.5	15-88	34	21-68	36	18-80	0.060	0.070
Group 2 (NMES)	37	16-72	48	24-78	41	23-93	**<0.001**	**<0.001**
HMS 90° (Nm)								
Group 1 (NMES+PNS)	25.5	16-60	30	15-62	36	13-61	**0.018**	**0.001**
Group 2 (NMES)	31	11-64	41	22-68	36	20-88	**<0.001**	**<0.001**
HMS 120° (Nm)								
Group 1 (NMES+PNS)	23	11-56	28	16-58	26.5	13-57	**0.022**	**0.046**
Group 2 (NMES)	28	16-51	34	19-55	30	18-65	**<0.001**	**<0.001**
WOMAC Pain								
Group 1 (NMES+PNS)	8	3-18	4	0-16	5	0-15	**<0.001**	**0.001**
Group 2 (NMES)	10	1-14	5	0-19	3	0-14	**0.003**	**<0.001**
WOMAC Stifness								
Group 1 (NMES+PNS)	2	0-6	1,5	0-5	2	0-4	0.556	**0.040**
Group 2 (NMES)	2	0-5	1	0-5	1	0-5	0.569	0.123
WOMAC Physical function								
Group 1 (NMES+PNS)	27	7-53	17	1-52	18	0-48	**0.006**	**<0.001**
Group 2 (NMES)	25	6-47	15	2-51	19	2-40	**0.001**	**<0.001**
WOMAC Total								
Group 1 (NMES+PNS)	40.1	10.4-79.1	23.4	3.1-75	24.5	0-69.8	**0.002**	**<0.001**
Group 2 (NMES)	40.6	8.3-63.5	25	3.1-74	25	2-58.3	**0.002**	**<0.001**
NHP Pain								
Group 1 (NMES+PNS)	52.3	25.2-100	27	0-100	31.7	0-80.2	**<0.001**	**<0.001**
Group 2 (NMES)	48.9	14.7-100	26	0-100	31.7	0-100	**0.007**	**0.013**
NHP Emotional reactions								
Group 1 (NMES+PNS)	57	0-92.7	38.4	0-92.7	22.1	0-100	0.375	**0.028**
Group 2 (NMES)	52.82	0-100	24.4	0-80.7	23.2	0-80.7	**<0.001**	**<0.001**
NHP Sleep								
Group 1 (NMES+PNS)	46.1	0-77.6	55.4	0-100	19.9	0-78.3	0.801	**0.043**
Group 2 (NMES)	27.2	0-77.6	27.2	0-77.6	12.5	0-77.6	0.668	0.968

TABLE 2
Continued

	Pre-treatment (W0)		Second week (W2)		Sixth week (W6)		W0-W2	W0-W6
	Median	Min-Max	Median	Min-Max	Median	Min-Max	*p*	*p*
NHP Social isolation								
Group 1 (NMES+PNS)	7.9	0-100	0	0-100	0	0-77.4	0.752	0.063
Group 2 (NMES)	22.5	0-58.1	15.9	0-44.5	0	0-64.67	0.590	0.271
NHP Physical activity								
Group 1 (NMES+PNS)	32.5	0-54.4	33	0-54.4	21.9	0-54.4	0.025	0.020
Group 2 (NMES)	41.8	10.7-67.1	21.9	0-46.1	21.9	0-54.4	<0.001	<0.001
NHP Fatigue								
Group 1 (NMES+PNS)	76	0-100	76	0-100	50	0-100	0.214	0.630
Group 2 (NMES)	63.2	0-100	60.8	0-100	60.8	0-100	0.216	0.157
NHP Total								
Group 1 (NMES+PNS)	278	72-512	241	0-512	162	10-446	0.001	<0.001
Group 2 (NMES)	239	111-476	98	46-392	190	36-365	<0.001	<0.001

VAS: Visual Analog Scale; NMES: Neuromuscular electrical stimulation; PNS: Peroneal nerve stimulation; QMS: Quadriceps muscle strength; HMS: Hamstring muscle strength; WOMAC: Western Ontario and McMaster Universities Arthritis Index; NHP: Nottingham Health Profile; Nm: Newton-meter.

Quality of life was assessed using the Nottingham Health Profile (NHP). It is a general quality of life questionnaire that measures patients' perceived health problems. The questionnaire consists of 38 items and assesses six dimensions related to health status: energy, pain, emotional reactions, sleep, social isolation, and physical activity. For each part, "0" indicates the best health condition and "100" indicates the worst health condition.[18]

Ambulation was measured using a walking test of 50×2=100 m. The patient was instructed to walk at the maximum speed they could attain without running, and the time required to do so was recorded in seconds.[19]

Statistical analysis

A sample size estimation was made using two groups. An online sample size calculator was used in the calculation of the sample size (https://www.danielsoper.com/statcalc/default.aspx), which determined that 28 individuals in each group were required to detect a large effect size (Cohen's d=0.80) with 0.80 statistical power and a 0.05 alpha level. This was calculated using previously published data showing a significant gain in muscle strength in the experimental group compared to the control group (Cohen's d>0.80).[20] As a result, 63 participants were initially included in this trial, which allowed for a 16% dropout rate.

Data analysis was performed using the IBM SPSS version 22.0 software (IBM Corp., Armonk, NY, USA). The chi-square test and Fisher test were used to compare categorical data. The conformity of the data to the normal distribution was evaluated using the Shapiro-Wilk test. The data showed nonnormal distribution. The Mann-Whitney U test was used for the comparison of groups. The Wilcoxon signed-rank test was used for within-group comparisons. The comparison of the treatment groups was made using intention-to-treat analysis of the difference between baseline and final scores with 95% confidence intervals using the Mann-Whitney U test. A p-value <0.05 was considered statistically significant.

RESULTS

Two patients from Group 1 and two patients from Group 2 were excluded from the study after they failed to show up for the six-week control (Figure 1). As a result, the study was completed with 59 patients (30 females, 29 males; mean age: 55.9±6.1 years; range, 40 to 65). There was no significant difference in terms demographic characteristics and initial evaluation parameters between the two groups (p>0.05, Table 1).

When the two-and six-week evaluations were compared for patients in Group 1, a significant improvement was observed in VAS scores, 100-m walking test, proprioception (30° and 60°), QMS (60°, 90°, and 120°), and HMS (60°, 90°, and 120°; p<0.05). A significant improvement was detected in VAS score and 100-m walking test score of the patients in Group 2 for both two- and six-week evaluations (p<0.05). A significant difference was detected in QMS (60°, 90°, and 120°) measurements at two-and six-week evaluations in Group 2 (p<0.05). Furthermore, there

was no significant increase in HMS (60°) value in two- and six-week evaluations in Group 2 ($p>0.05$). However, a significant increase was detected in two- and six-week evaluations of HMS (90° and 120°) values ($p<0.05$, Table 2).

A significant improvement was found in WOMAC pain scores of both groups in two-and six-week evaluations ($p<0.05$). There was a significant improvement in WOMAC functionality and WOMAC total scores of both groups in two- and six-week evaluations ($p<0.05$).

In terms of NHP scores, there was a significant improvement in NHP pain scores, NHP physical activity, and NHP total scores of both groups in two-and six-week evaluations ($p<0.05$).

When VAS scores, QMS data, and WOMAC scores were examined, there was no significant difference between the two groups ($p>0.05$). While there was no significant difference between the two groups in the 100-m walking test score in the two-week evaluation ($p>0.05$), there was a significant difference in favor of Group 2 in the six-week control ($p<0.05$). There was a significant difference in favor of Group 1 in proprioception (30° and 60°) and HMS (60° and 90°) parameters in two-and six-week evaluations ($p<0.05$). While there was no significant difference in the HMS (120°) score in the two-week control ($p>0.05$), a significant difference was observed in favor of Group 1 in the six-week control ($p<0.05$). With regard to NHP scores, while there was a significant difference in favor of Group 1 in both two-and six-week evaluations of NHP emotional reaction scores ($p<0.05$), there was no significant difference between the groups for all other NHP scores ($p>0.05$, Table 3).

DISCUSSION

Studies have shown that NMES increases muscle strength, improves functional status, and can prevent immobilization-induced muscle atrophy.[15,21-23] In our study, we used NMES for both groups, and similar to other studies in the literature, we found a significant increase in QMS in both groups. In addition, both groups showed a significant improvement in physical activity scores and functionality parameters, as well as a decrease in pain intensity. Studies investigating the effect of PNS on arthrogenic muscle inhibition are limited and mostly focused on the quadriceps.[10] Peroneal nerve stimulation is thought to prevent arthrogenic muscle inhibition by preventing the transmission of inhibitory signals to quadriceps' alpha motor neurons.[10] Thus, muscle atrophy and loss of muscle strength can be reduced. The immediate effect of electrical stimulation of the peroneal nerve on arthrogenic inhibition in the quadriceps muscle was investigated in a study including 15 patients.[10] Arthrogenic muscle inhibition was measured using the central activation rate. This rate was obtained by dividing the extension force without nerve stimulation by the extension force during stimulation. When the two stages of this study were compared, a significant increase in muscle strength was detected in the stage where PNS was performed. With these findings, the central activation rate was found to be lower in the second stage. Unlike previous studies, we evaluated QMS at the end of the treatment (second week) and at the six-week control rather than evaluating it instantaneously. We also planned to evaluate HMS since the peroneal nerve is a branch of the sciatic nerve and the hamstring muscles are innervated by the branches of the sciatic nerve. We did not observe a significant increase between the groups in terms of QMS, but in terms of HMS, a significant increase was observed in all parameters in favor of Group 1 in both two-and six-week evaluations. This suggests that in patients with knee OA, atrophy and loss of strength may develop due to arthrogenic muscle inhibition at significant levels in the hamstring group, and the effect of PNS on arthrogenic muscle inhibition may be greater in the hamstring group than in the quadriceps group.

Studies have demonstrated that knees with a low hamstring-to-quadriceps strength ratio have a higher risk of anterior cruciate ligament (ACL) injury.[24-26] Osteoarthritis is a complication in the knee joint that can develop over time due to ACL injuries. After an ACL injury, the incidence of knee OA increases by 15 to 20%.[27] In addition, it has been suggested that more than half of the patients with ACL injuries develop symptomatic OA within 20 years.[28] In our study, the therapy group had a considerable improvement in HMS. These results suggest that administering PNS in addition to muscle strengthening therapies in the early period may increase the success of knee stabilization and rehabilitation in patients with OA and ACL tears and in patients undergoing surgery after an ACL injury.

Two studies show that the sense of proprioception is impaired in patients with knee OA.[29,30] With the decrease in the sense of proprioception, rhythmic

TABLE 3
Comparison of the difference scores between the groups

	Second Week					Sixth Week				
	Group 1 (NMES+PNS)		Group 2 (NMES)			Group 1 (NMES+PNS)		Group 2 (NMES)		
	Median	Min-Max	Median	Min-Max	*p*	Median	Min-Max	Median	Min-Max	*p*
Visual Analog Scale	–2.5	–6 - –1	–2	–6 - 1	0.247	–2	–5 - 3	–2	–6 - 2	0.190
100 meter walk test	–3	–12 - 1	–6.5	–15 - 5	0.456	–4	–20 - 6	–6.5	–26 - 0	0.006
Proprioception 30° (0)	–1	–23.34 - 9.67	–8	–25.33 - 6	0.025	–1.48	–28.66 - 10.67	–8.67	–30.66 - 6	0.003
Proprioception 60° (0)	–1	–12 - 12	–4	–16 - 14	0.011	–2.16	–11.33 - 14.67	–4	–15 - 8	0.039
QMS 60° (Nm)	8	–31 - 51	6	–12 - 44	0.958	5	–42 - 51	10	–18 - 56	0.575
QMS 90° (Nm)	4	–35 - 36	6	–7 – 43	0.814	8.5	–45 - 46	8	–16 - 43	0.638
QMS 120° (Nm)	8.5	–14 - 38	5	–24 - 31	0.187	8	–23 - 34	6	–20 - 36	0.362
HMS 60° (Nm)	3	–13 - 32	10	–8 - 37	0.021	4	–11 - 32	8	–7 - 45	0.029
HMS 90° (Nm)	4	–11 - 16	8	–7 - 35	0.032	5	–5 - 16	10	–23 - 55	0.043
HMS 120° (Nm)	3	–14 - 16	3	–18 - 23	0.172	1.5	–15 - 8	6	–15 - 29	0.030
WOMAC Pain	–2	–7 - 4	–2	–7 - 7	0,819	–3	–11 - 6	-3	–9 - 2	0.873
WOMAC Stiffness	0	–5 - 3	0	–3 - 3	0.963	–1	–4 - 3	0	–4 - 4	0.558
WOMAC Physical function	–3	–28 - 10	–8	–23 - 16	0.554	–22.5	–43 - –1	–21	–36 - –5	0.606
WOMAC Total	5.2	–37.5 - 14.5	12.5	–31.2 - 20.8	0.727	–15.6	–45.8 - 20.8	–12.5	–40.6 - 21.8	0.519
NHP Pain	–21.9	–49.2 - 30.2	–16	–50.4 - 31.3	0.113	–30.1	–63.5 - 33.7	–17	–59.4 - 54.2	0.057
NHP Emotional reactions	0	–36 - 33	–13.9	–74 - 33	0.001	–3.6	–69.8 - 25.5	–19.2	–59 - 13	0.038
NHP Sleep	0	–27.2 - 34.2	0	–77.6 - 55.9	0.67	–6.2	–65 - 48.9	0	–65 - 55.9	0.118
NHP Social isolation	0	–44.5 - 22.5	0	–58.1 - 22.5	0.382	0	–57.8 - 22.5	0	–58.1 - 42.1	0.667
NHP Physical activity	0	–43.6 - 19.8	–11.2	–23.8 - 19.8	0.98	–9.4	–43.6 - 21.9	–19.8	–31 - 19.8	0.316
NHP Fatigue	0	–60.8 - 39.2	–2.4	–39.2 - 60.8	0.405	0	–100 - 60.8	0	–39.2 - 63.2	0.176
NHP Total	–38.2	–138.6 - 30.2	–66.1	–171.4 - 77.3	0.278	–73.8	–299.2 - 179.2	–74.6	–299.2 - 179.2	0.426

NMES: Neuromuscular electrical stimulation; PNS: Peroneal nerve stimulation; QMS: Quadriceps muscle strength; HMS: Hamstring muscle strength; Nm: Newton-meter; WOMAC: Western Ontario and McMaster Universities Arthritis Index; NHP: Nottingham Health Profile.

walking becomes more difficult, stride distance becomes shorter, and walking speed decreases. As a result, the functionality decreases.[30] It has been demonstrated that when proprioception improves, functional capacity increases and pain decreases in patients with knee OA.[31] Levinger et al.[32] investigated patients who had total knee arthroplasty for knee OA before and one year after the operation. Patients' pain, stiffness, functional limitation, and muscle strength all improved significantly one year after the operation, but their proprioception did not improve. A study investigated the effect of elastic bandages on pain and proprioception in patients with knee OA, and while the elastic bandage was effective on VAS pain score, it had no effect on proprioception.[33] There is no research on the effect of PNS on knee proprioception in patients with knee OA in the literature. In our study, the treatment group showed a significant improvement in all parameters used to assess proprioception, both in the two-and six-week evaluations. This suggests that the application of PNS may be beneficial in correcting impaired proprioception in patients with knee OA and may increase the gait speed and functionality of these patients.

The strength of our study is that it is the first study to examine the effects of PNS on QMS, HMS, and proprioception together in patients with knee OA using an isokinetic device. Our study may serve as a guide for future research on this subject. Moreover, the VAS,[11] WOMAC,[20] and NHP,[12] which we used to assess patients, are scales that have been used in several studies investigating patients with knee OA.

The limitation of our study is the small number of patients included, and further research with a large number of patients is needed to generalize the findings.

In conclusion, our findings suggest that PNS combined with NMES could be more effective for the treatment of patients with knee OA in terms of proprioception, HMS, and functional status.

Ethics Committee Approval: The study protocol was approved by the Bursa High Specialization Training and Research Hospital Clinical Research Ethics Committee (date: 23.11.2011, no: KAEK-25 2019/12-19). The study was conducted in accordance with the principles of the Declaration of Helsinki.

Patient Consent for Publication: A written informed consent was obtained from each patient.

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

Author Contributions: Idea design, data collection and processing, writing manuscript, references and literature review: Ö.Y.; Idea design,analysis,control/Supervision and critical review: M.K.A.

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